PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 01 November 2000 (01.11.00)	
International application No. PCT/FI00/00227	**Applicant's or agent's file reference** åp2820
International filing date (day/month/year) 20 March 2000 (20.03.00)	**Priority date** (day/month/year) 29 March 1999 (29.03.99)
Applicant KÄKÖNEN, Sanna-Maria et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

29 September 2000 (29.09.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

Th International Bureau f WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Charlotte ENGER
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
åp2820		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/FI00/00227	20.03.2000	29.03.1999
International Patent Classification (IPC) or national classification and IPC7		
G01N 33/68		
Applicant		
Käkönen, Sanna-Maria		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.09.2000	13.07.2001
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Telex: 17978 PATOREG-S Facsimile No. 08-667 72 88	Authorized officer Carl-Olof Gustafsson/EÖ Telephone No. 08-782 25 00

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FI00/00227

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement) under article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheet/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2 (c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FI00/00227

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-8, 15	YES
	Claims	9-14	NO
Inventive step (IS)	Claims		YES
	Claims	1-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The present invention relates to a method and a kit for the assessment of bone fragility and fracture risk or osteoporosis by measuring gamma carboxylated osteocalcin (COC) and comparing the level with the normal level of COC. Alternatively the COC level to total osteocalcin (TOC/IOC) level ratio is compared to the ratio of the corresponding mean COC level to mean TOC/IOC levels.

The following documents are considered to be of particular relevance and were cited in the International Search Report:

D1 EP557663, see p 4, l 30 - p5, l 10, p 6-7 and claims
D2 J. Bone Mineral. Res. Vol. 14(4), 1999, p 555-60 (BIOSIS acc. no 1999:240702), probably published after priority date of the application.
D3 J. Immunol. Meth. Vol. 139, 1991, p 17-23 (BIOSIS acc. no 1991:92041118)
D4 Calcific. Tissue. Int. Vol. 62, 1998, p 286-89 (BIOSIS acc. No 1998:206737
D5 WO9909058
D6 DE4008546

D1 relates to a method and a kit for the assessment of bone fragility and osteoporotic fracture risk. The document focus on estimation of the "under-carboxylated" (ucOC) fraction of OC compared with the "normal level" of OC and teaches that the measurement of the non-carboxylated fraction or the ration of this fraction to TOC is the disease-discriminating part of the OC (see p 7); see also the present application p 3, l 25 ff.

.../...

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: V

D3 (fig 4) correlates the level of COC (=Gla-OC) of e.g. osteoporosis subjects with "normal levels" of COC with the aid of COC specific monoclonal antibodies. The document seems to refer to a "normal level" that can be a mean level of COC not correlated for age (sex?). As the importance of such considerations have been recognised (see the present application p 3-4) it would be obvious to a person skilled in the art to modify the method according to D3 by comparing the COC measurements with the mean COC level of a group with the same age and sex. Consequently, the method is considered to lack an inventive step.

D4 discuss the importance of ucOC levels compared to total OC (p 288) and arrives at results similar to those obtained in D1.

D5 and D6 reveal the use of monoclonal antibodies specific to carboxylated osteocalcin in immunoassays.

The kit according to claims 9-14 is considered to lack novelty over the cited documents.

Taking into account the recent knowledge about the age and sex related changes of the different forms of OCs and the disease-discriminating comparison of COC (Gla-OC) level to normal levels of COC (D3), it would be obvious to a person skilled in the art to investigate the ratio of COC to TOC/IOC as well. Immunochromatography is a well-known technique that would be obvious to a person skilled in the art to apply in assays for COC and similar compounds. Therefore, in the absence of a reasoned statement from the applicant and lack of unexpected advantages, the method according to claims 1-8 and any novel aspect of the kit according to claims 9-15 are considered to lack an inventive step.